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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/622,124	07/18/2003	Martin F. Bachmann	1700.0340001/BJD/SJE	3313

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STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.
1100 NEW YORK AVENUE, N.W.
WASHINGTON, DC 20005

EXAMINER

BOESEN, AGNIESZKA

ART UNIT	PAPER NUMBER
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1648

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10/15/2009

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/622,124	Applicant(s) BACHMANN ET AL.	
	Examiner AGNIESZKA BOESEN	Art Unit 1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 04 August 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 63,68-76,78-88,94,97-116,118-123,126 and 128-139 is/are pending in the application.
- 4a) Of the above claim(s) 74,99,105-107,111-113,121-123 and 133 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 63, 68-73, 75, 76, 78-88, 94, 97, 98, 100-104, 108-110, 114-116, 118-120, 124, 126, 128-132 and 134-139 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on August 4, 2009 has been entered.

Claims 63, 68-73, 75, 76, 78-88, 94, 97, 98, 100-104, 108-110, 114-116, 118-120, 124, 126, 128-132 and 134-139 are under consideration in this Office action.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Rejection of claims 63, 68-73, 75, 76, 78-88, 94, 97, 98, 100-104, 108-110, 114-116, 118-120, 124, 126, 128-132 and 134-139 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stockley et al. (US Patent 6,159,728) in view of Deghengi et al. (US 2002/0187938), Kojima et al. (Nature, 1999 Vol. 402, p. 656-660) Maita et al. (Gen Pept Accession VCBPQB, 1971) and further in view of Nielsen et al. (US Patent 6,548,651 B1) **is maintained.**

Applicant's arguments have been fully considered but fail to persuade. Applicants argue that the cited references do not disclose or suggest a composition comprising a virus-like particle with at least one first attachment site "wherein said first attachment site is a lysine residue of said virus-like particle and said second attachment site is a cysteine residue" as recited in the present claims.

Applicant states that "The disclosure of Nielsen relates to peptide nucleic acid (PNA) sequences that are modified in order to obtain PNA molecules which exhibit anti-infective properties. See Nielsen column 1, lines 26-29. Specifically, Nielsen discloses that the PNA molecules are modified by linkage to a peptide or peptide-like sequence that enhances the activity of the PNA. Nielsen further discloses that the PNA molecule may be connected to the peptide moiety either by direct binding or by a linker. See, Nielsen column 7, lines 66-67. In the instances where a linker is used, the linker may be used as a single linking group or together with more groups, and different linking groups can be combined in any order and number. See, Nielsen at column 8, lines 21-25. Finally, Nielsen discloses that the peptide may be linked to the PNA sequence via either the amino or carboxy end, an internal part of the peptide, or alternatively, both the amino and carboxy ends. See, Nielsen at column 8, lines 42-46. Nielsen discloses that the modified PNA molecules form "a pattern comprising positively charged and lipophilic amino acids or amino acid analogues." See, Nielsen at column 3, lines 53-55.

Applicant argues that "In contrast to Nielsen, the presently claimed invention provides compositions comprising a virus-like particle of an RNA-bacteriophage to which ghrelin antigens are associated through specific non-peptide covalent bonds, and wherein said association is effected by way of lysine residues of virus-like particles of an RNA-bacteriophage

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and cysteine residues of the ghrelin antigens as second attachment sites. The specific attachments of the ghrelin antigens by way of cysteine residues to lysine residues of the virus-like particle of an RNA- bacteriophage result in highly ordered and repetitive ghrelin arrays that represent potent immunogens for the induction of immune responses against ghrelin. See, the present specification at paragraphs [0183] - [0188].

Applicant argues that there is no disclosure in Nielsen that would have led the skilled artisan to modify the structure of Stockley in order to prepare the compositions of the presently claimed invention. Applicant argues that the Examiner's contention that "SMPH is a suitable linker for attachment of peptides with nucleic acids" is insufficient to cure the deficiencies of Stockley, Deghenghi, Kojima and Maita.

In response to Applicant's arguments the Examiner notes that all the elements of the claimed invention are taught in the prior art, as discussed on the record (see (Non-final Office action on 4/16/2008 and Final Office action on 2/4/2009). Stockley teaches pharmaceutical compositions comprising virus like particles of an RNA bacteriophage, particularly the Q β bacteriophage as an antigen delivery system (see the entire document, particularly claims 1-12). Stockley teaches the non-peptide covalent coupling between the RNA bacteriophage and the antigen of interest (see column 3, lines 22-44, column 12, lines 8-29 and claim 8). Maita teaches coat protein of Q β bacteriophage having a sequence identical with present SEQ ID NO: 4 (see page 2 of Maita's reference). Neither Stockley nor Maita teach that the peptide to be delivered is a ghrelin peptide. Deghenghi teaches administration of ghrelin peptides in a mammal to reduce the growth hormone release (see the entire document, particularly claims 1-18 and Examples 1-3). The ghrelin peptide sequences disclosed by Deghenghi comprise presently claimed SEQ ID

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NO: 119 (see Example 1 and claims 1, 2, and 11). Deghenghi does not teach ghrelin peptides of SEQ ID NO: 31 and SEQ ID NO: 65. Kojima cures this deficiency in that Kojima teach a human ghrelin peptide, which sequence is identical with the instantly claimed SEQ ID NO: 31 (see page 658, Figure 4, ghrelin sequence is boxed). The ghrelin peptide of SEQ ID NO: 65, with the second attachment site, is exactly the same peptide as SEQ ID NO: 31 except that peptide of SEQ ID NO: 65 has an additional cysteine residue on the amino terminus. It is herein interpreted that the cysteine residue on the C terminal of the ghrelin peptide serves as the attachment site.

Nielsen et al. teach a non-peptide heterobifunctional cross-linker succinimidyl 6-(β -maleimido-propionamido) hexanoate (SMPH) covalently linking peptides with nucleic acid molecules representing bacterial antigens through either a cysteine (C) or a lysine (K) residue (see claim 1, Tables 1 and 4, column 8, lines 17-41 and column 9, lines 4-10).

It would have been *prima facie* obvious to the person of ordinary skill in the art to covalently attach Stockley's RNA Q β bacteriophage to Deghenghi's and/or Kojima's ghrelin peptide using Nielsen's non-peptide heterobifunctional cross-linker succinimidyl 6-(β -maleimido-propionamido) hexanoate (SMPH) capable of reacting with the first attachment site which is a lysine residue and a second attachment site which is a cysteine residue because Nielsen teaches that the SMPH is a suitable linker for attachment of peptides with nucleic acids (see claim 1, Tables 1 and 4, column 8, lines 17-41 and column 9, lines 4-10).

One would have been motivated to use Nielsen's succinimidyl 6-(β -maleimido-propionamido) hexanoate (SMPH) linker to attach Deghenghi's and/or Kojima's ghrelin peptide to Stockley's RNA Q β bacteriophage because Nielsen teaches that the SMPH linker is used to attach peptides and nucleic acid molecules together.

Thus the present claims would have been obvious because the **combination** of one known element Stockley's RNA Q β bacteriophage, to Deghenghi's and/or Kojima's ghrelin peptide using and Nielsen's non-peptide heterobifunctional cross-linker succinimidyl 6-(β -maleimido-propionamido) hexanoate (SMPH) would have yielded predictable results to one of ordinary skill in the art at the time of the invention (i.e generation of a RNA Q β bacteriophage linked to the ghrelin peptide with non-peptide heterobifunctional cross-linker succinimidyl 6-(β -maleimido-propionamido) hexanoate (SMPH)). See *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385 (U.S. 2007).

The present claims would have been obvious because the **substitution** of one known element PNA molecules and peptide sequences, taught by Nielsen for another Stockley RNA bacteriophage and Deghenghi's and/or Kojima's ghrelin peptide, would have yielded predictable results to one of ordinary skill in the art at the time of the invention (i.e. a ordered and repetitive antigen array comprising VLP RNA bacteriophage and a ghrelin peptide). See *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385 (U.S. 2007).

Absent any unexpected results, it would have been *prima facie* obvious to the person of ordinary skill in the art to covalently attach Stockley's RNA Q β bacteriophage to Deghenghi's and/or Kojima's ghrelin peptide using Nielsen's non-peptide heterobifunctional cross-linker succinimidyl 6-(β -maleimido-propionamido) hexanoate (SMPH) capable of reacting with the first attachment site which is a lysine residue and a second attachment site which is a cysteine residue

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All the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Thus in view of the foregoing the rejection is maintained.

New Rejection

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 63, 68-73, 75, 76, 78-88, 94, 97, 98, 100-104, 108-110, 114-116, 118-120, 124, 126, 128-132 and 134-139 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-23 of copending

Application No. 11/663,350. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of this application and the claims of the copending application are drawn to a VLP RNA bacteriophage conjugated to a ghrelin peptide.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 63, 68-73, 75, 76, 78-88, 94, 97, 98, 100-104, 108-110, 114-116, 118-120, 124, 126, 128-132 and 134-139 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 2, 4, 8, 13-23, 25 and 36-51 of copending Application No. 11/664,716.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of this application and the claims of the copending application are drawn to a VLP RNA bacteriophage conjugated to a ghrelin peptide.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to AGNIESZKA BOESEN whose telephone number is (571)272-8035. The examiner can normally be reached on Monday – Friday from 9:00 AM to 6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Agnieszka Boesen/

Examiner, Art Unit 1648